The importance of the Biostatistics Collaboration of Australia

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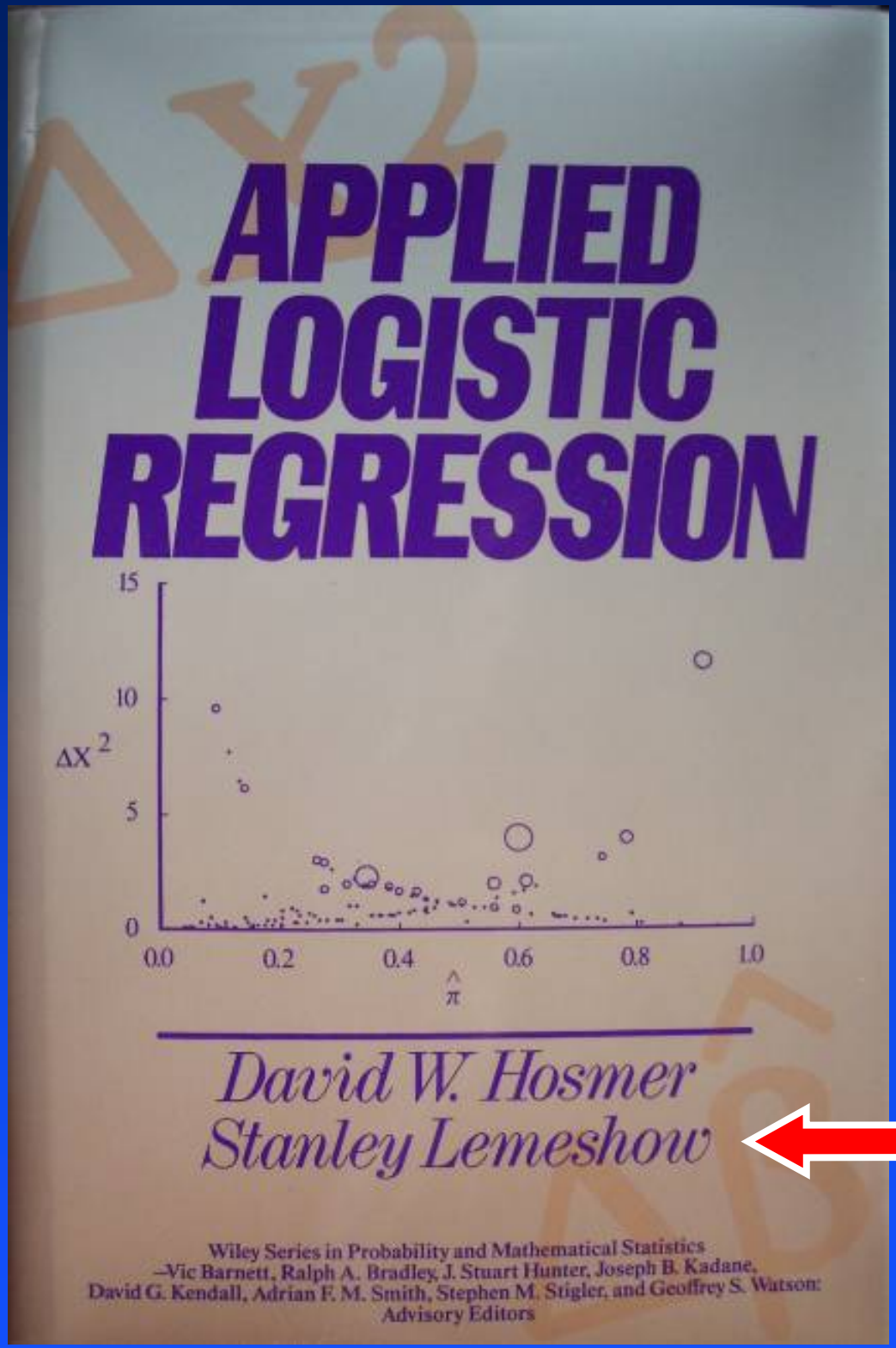

- First edition 1989
- 19 years ago!

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1.5 The ICU Study

A data set which will be used in exercises throughout the text consists of a sample of 200 subjects who were part of a much larger study on survival of patients following admission to an adult intensive care unit (ICU). The major goal of this study was to develop a logistic regression model to predict the probability of survival to hospital discharge of these patients. A number of publications have appeared which have focused on various facets of the problem. The reader wishing to learn more about the clinical aspects of this study should start with Lemeshow, Teres, Avrunin, and Pastides (1988). A code sheet for the variables to be considered in this text is given below in Table 1.4. A listing of the data is provided in Appendix 2.

Table 1.4 Code Sheet for the ICU Data.

	Column Heading

JAMA®
The Journal of the American Medical Association

1993: logistic regression ICU severity-of-illness score

- Simplified Acute Physiology Score (SAPS II)
  - 17-variable score predicting hospital mortality developed and validated using 13,152 admissions to 137 adult medical/surgical ICUs in 12 countries
- ***Goodness-of-fit tests***
  - model performed well
- CONCLUSION
  - SAPS II risk-of-death estimates useful
  - a starting point for future evaluation of ICU efficiency

Le Gall JR, Lemeshow S, Saulnier F.
***JAMA* 1993 Dec 22-29;270(24):2957-63**

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Hosmer-Lemeshow Goodness–of-fit test

- Amateur attempts at logistic regression with push-button software
- Unable to read mathematics
- Minimal understanding of underlying model
- $1000s spent on statistical “advice”
- 18 months to find someone to assess fit of logistic model using H-L test
- 5 minutes using Stata (version 5)

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The problem continues…

- Statistics is a difficult topic to teach and learn and there is ample evidence that its application is often faulty in medicine as well as in many other scientific disciplines. Errors include aspects of design, analysis, reporting and interpretation

García-Berthou E, Alcaraz C.
BMC Medical Research Methodology 2004, 4:13.

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The problem continues…

- "Much research is done without the benefit of anyone with adequate training in quantitative methods."
- "Many investigators are not professional researchers; they are primarily clinicians"

Altman DG. Poor-Quality Medical Research. What Can Journals Do?
***JAMA* 2002;287:2765-2767**

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Success of the BCA

- Delivered entirely by distance education
- Provide background in mathematical and statistical theory to those without a first degree in mathematics or statistics
- Fills the gap between public health /epidemiology and general statistics courses
- Taught well by enthusiasts

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My Graduate Activities

- Teaching clinical students
- ANZICS CTG
  - Australian and New Zealand Intensive Care Society Clinical Trials Group
- Workplace project
- “In-house” statistical analyses
  - Supervision of PhD student
  - Other research publications

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About the ANZIC-RC

Over the last 5 to 10 years the intensive care community of Australia and New Zealand has built a track record and solid reputation for the conduct of high quality, investigator initiated clinical research concerning the diseases and treatments that affect critically ill patients. Since 2001, ANZICS CTG investigators have received consecutive annual Australian NHMRC Project Grant funding for multi-centre clinical trials totaling over $5.2M. In the same time, they have been awarded a total of $8.8M in competitive grant monies. This track record has been developed through individual achievement in addition to the highly productive collaborative activities of the ANZICS-CTG, formed in 1994. Since then, the ANZICS CTG has completed and published high impact studies of increasing complexity and size. These include the 'low dose dopamine trial for patients with early acute renal failure' (n=328, *The Lancet 2000*), the 'Saline Albumin Fluid Evaluation (SAFE) study' (n=6997; *NEJM 2004*), and the 'Medical Early Response Intervention and Therapy (MERIT) study' (Cluster RCT of 23 hospitals, *The Lancet 2005*). The Level I evidence emerging from these trials has improved clinical practice internationally.

In October 2005, $1.29 million dollars in funding was received in the form of an NHMRC Enabling Grant to establish a national centre for intensive care research.

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AUSTRALIAN AND NEW ZEALAND INTENSIVE CARE SOCIETY

ANZICS

Clinical Trials Group

About the Clinical Trials Group

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ANALYSIS OF OUTCOME FOLLOWING SEVERE TRAUMATIC BRAIN INJURY

- Double-blind, randomized, controlled trial of 226 patients with severe traumatic brain injury
- Project explored additional statistical and clinical aspects of outcome analyses and sample size
  - ordered categories rather than traditional dichotomy
  - ordinal logistic regression (proportional odds)
  - power and sample size for 8-level ordinal outcomes

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A randomized trial of protocol-directed sedation management for mechanical ventilation in an Australian intensive care unit*

Tracey K. Bucknall, RN, ICU Cert, BN, Grad Dip Adv Nurs, PhD, MRCNA;
Elizabeth Manias, RN, CertCritCare, BPharm, MPharm, MNStud, PhD, FRCNA;
Jeffrey J. Presneill, MBBS, PhD, FRACP, FJFICM

Objective: To compare protocol-directed sedation management with traditional non-protocol-directed practice in mechanically ventilated patients.

Design: Randomized, controlled trial.

Setting: General intensive care unit (24 beds) in an Australian metropolitan teaching hospital.

Patients: Adult, mechanically ventilated patients (n = 312).

Interventions: Patients were randomly assigned to receive sedation directed by formal guidelines (protocol group, n = 153) or usual local clinical practice (control, n = 159).

Measurements and Main Results: The median (95% confidence interval) duration of ventilation was 79 hrs (56–93 hrs) for patients in the protocol group compared with 58 hrs (44–78 hrs) for patients who received control care (p = .20). Lengths of stay (median [range]) in the intensive care unit (94 [2–1106] hrs vs. 88 (14–962) hrs, p = .58) and hospital (13 [1–113] days vs. 13 (1–365) days, p = .97) were similar, as were the proportions of subjects receiving a tracheostomy (17% vs. 15%, p = .64) or undergoing unplanned self-extubation (1.3% vs. 0.6%, p = .61). Death in the intensive care unit occurred in 32 (21%) patients in the protocol group and 32 (20%) control subjects (p = .89), with a similar overall proportion of deaths in hospital (25% vs. 22%, p = .51). A Cox proportional hazards model, after adjustment for age, gender, Acute Physiology and Chronic Health Evaluation II score, diagnostic category, and doses of commonly used drugs, estimated that protocol sedation management was associated with a 22% decrease (95% confidence interval 40% decrease to 2% increase, p = .07) in the occurrence of successful weaning from mechanical ventilation.

Conclusions: This randomized trial provided no evidence of a substantial reduction in the duration of mechanical ventilation or length of stay, in either the intensive care unit or the hospital, with the use of protocol-directed sedation compared with usual local management. Qualified high-intensity nurse staffing and routine Australian intensive care unit nursing responsibility for many aspects of ventilatory practice may explain the contrast between these findings and some recent North American studies. (Crit Care Med 2008; 36:1444–1450)

Key Words: ventilator weaning; clinical decision making; clinical protocols; intensive care; outcome and process assessment (health care); hypnotics and sedatives

Critical Care Medicine 2008:36:1444-1450

Statistical review of manuscript

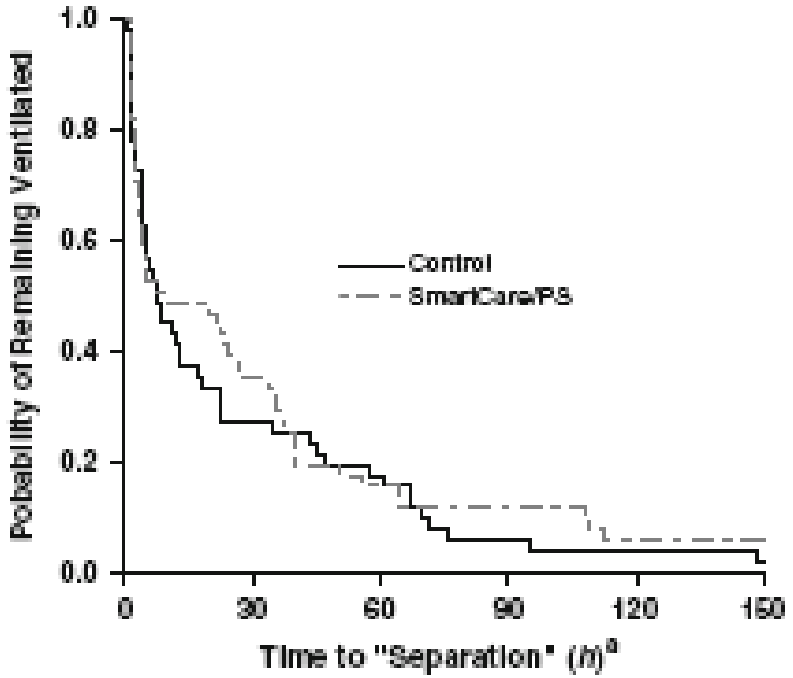
- 28 pages of background statistical analysis and commentary
  - included a variety of exploratory analyses
  - extensive checks of assumptions
  - examination of the "competing risks" issue
- “The paper…exceeds the standard of statistical presentation of most papers I see.”

Intensive Care Med
DOI 10.1007/s00134-008-1179-4

ORIGINAL

Louise Rose
Jeffrey J. Presneill
Linda Johnston
John F. Cade

A randomised, controlled trial of conventional versus automated weaning from mechanical ventilation using SmartCare™/PS



Number at risk						
SmartCare/PS	51	19	9	7	4	4
Control	51	15	10	4	3	2

Fig. 2 Kaplan–Meier estimated probability of remaining ventilated. Log-rank test $P = 0.3$. Plot truncated at 150 h due to small numbers of patients beyond that point. [a] Time in hours from randomisation to the time of declaration of "separation potential"

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Annals of Internal Medicine 03 June 2008

Association between critical care physician management and patient mortality in the ICU

- North American ICUs: two clinical approaches
  - Specialist vs non-specialist
- 100,000 patient database
- Random effects logistic regression (123 ICUs)
- Severity of illness adjustment (expanded SAPS II)
- Propensity score (likelihood of selection for specialist)
  - Observational data – causal effects
- Stratified analyses (significant interactions)
- CONCLUSION
  - Adjusted mortality higher!

    Main effects model *OR* = 1.40 (95% CI 1.32–1.49)
  - True, or residual confounding? Anyone for an RCT?

Levy MM, Rapoport J, Lemeshow S, et al.
***Ann Intern Med* 2008;148(11):801-809**

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